

REMARKS

Claims 1 – 6, 8 – 22, 25 – 29 and 31 - 33 are pending in the application. Claim 1 has been amended. New claim 35 has been added. No new matter has been added by virtue of the claims or amendment, support being found throughout the specification and from the pending claims.

The Examiner indicates that non-initials or non-dated alterations have been made to the oath or decalaration. The Examiner points to 37 CFR 1.52(c). Applicants direct the Examiner to the language of 37 CFR 1.52(c) which states that:

Any interlineations, erasure, cancellation or other alteration of the application papers filed must be made before the signing of any accompanying oath or declaration...and should be dated and initialed or signed by the applicant on the same sheet of paper.

Inventor Moscho has made changes to his post office address and has also signed and dated the declaration, in accordance with 37 CFR 1.52(c).

Claim Rejections- 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 1 – 6, 8 – 29 and 31 – 33 under 35 USC, first paragraph, because the specification, while being enabling for *in vitro* selective electrofusion of at least two fusion partners having cell-like membranes, does not reasonably provide enablement for *in vivo* electrofusion of two fusion partners, or for conducting *in vitro* fertilization by selective electrofusion of an egg or an enucleated egg cell, and a sperm cell at any developmental stage, or for conducting human cloning. Applicants respectfully traverse the rejection.

Solely for the sake of advancing prosecution and allowance of the claims, and because the Examiner has indicated that the specification is “enabling for *in vitro* selective electrofusion of at least two fusion partners having cell-like membranes (Office Action, p.2), Applicants have amended claim 1 to recite an *in vitro* method for selective electrofusion of at least two fusion partners having cell-like membranes.

As the Examiner indicates, the invention is enabled for *in vitro* selective electrofusion of at least two fusion partners having cell-like membranes.

Applicants wish to point out that, according to the invention as currently claimed, it would not require a great deal of work to perform an *in vitro* method for selective electrofusion

of at least two fusion partners having cell-like membranes. The specification provides teaching of electrical field strength and number (p.8), strength and duration of fusion pulse (p.8), positioning of the electrodes (p.9), and preferred dimension of the electrodes (p.9). The specification teaches preparation of fluorescence encapsulated vesicles for use in the method (p.16), and chemicals and materials needed to perform the method (p.17 – 18). The specification provides examples of experimental setup and instrumentation (p.14 – 15). The specification provides working examples of both cell-cell and cell-liposome fusion (p.18 – 21).

In *In re Wands*, the court stated that “[e]nabling is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. ‘The key word is ‘undue’ not ‘experimentation’ (citing *In re Angstadt*, 537 F. 2d 498 at 504, 190 U.S.P.Q. 214 at 219 (C.C.P.A. 1976)). The Court also stated that “the test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.” (citing *In re Jackson*, 217 U.S.P.Q. 804 at 807 (Bd. App. 1982)), emphasis added. Thus, the instant specification provides ample guidance to perform an *in vitro* method for selective electrofusion of at least two fusion partners having cell-like membranes. Any experimentation required to perform the method using, for example, any two fusion partners having cell-like membranes in an *in vitro* environment would not require more than routine experimentation.

Applicants respectfully request withdrawal of the rejection and allowance of the claims.

Claim Rejections- 35 U.S.C. § 102(b)

Claims 1 and 17 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Magae et al. (Appl. Micro. Biotechol., 1986, Vol 24, 509-511). The Examiner argues that the Magae et al. reference teaches a method to fuse two giant plant protoplasts by using two glass electrodes prepared from glass capillaries and attached to a micromanipulator. The Examiner further alleges that the Magae et al. reference “meets the limitation of a highly focused electric field (Office Action, p. 11).” Applicants respectfully traverse the rejection.

The Examiner argues that “the disclosure does not provide a specific definition of the phrase ‘highly focused’ that would exclude the method taught by Magae et al. (Office Action,

p.10)." Applicants submit that the meaning of the term "highly focused" is well-supported and described in the specification. For example, on page 8, lines 30 – 37, the specification teaches:

The electrical field used in step B to obtain fusion should be *highly focused in order to avoid affecting any surrounding structures*...To focus the electrical field it is preferable to provide the electrical field by use of one or two microelectrodes positioned close to the two fusion partners, i.e. 0 – 10 μm , preferably 0 – 5 μm , from the cellular membrane. (emphasis added)

The term "highly focused" is made even clearer when read in light of the preceding paragraphs on page 8 that describe how the electrical field is obtained (lines 8 - 30), as well as the Examples. In particular, Example 3 (p.22) teaches positioning for cell fusion using single open-bore capillaries, and specifically positioning of the capillary tip using micromanipulators and fusion of two aligned cells by applying pulses of 5 to 15 kV for 0.1 – 5 seconds.

As the Examiner states, the Magae et al. reference teaches that "the electrofusion of plant protoplasts occurs in a drop of protoplast solution on a cover glass and results in the fusion of 10 to 20 pairs of protoplasts (Office Action, p.10)." Specifically, the Magae et al. reference teaches on page 509 that, "fusion frequency was estimated as the number of fused protoplasts that had achieved the final stage; that is a completely spherical form, *among 10 to 20 pairs of protoplasts* (emphasis added)." Contrary to the Examiner's assertion, the method of Magae et al. does not meet the limitation of electrofusion of at least two fusion partners using a highly focused electric field, but rather teaches bulk fusion of structures in a solution. The Magae et al. reference fails to teach a method of fusion that is highly focused in order to avoid affecting any surrounding structures, but rather teaches a method of fusion whereby structures in a protoplast solution are induced to fuse in an un-focused manner.

Moreover, as Applicants stated in the previous response, Magae et al. teach a method to fuse two giant plant protoplasts using glass electrodes attached to a micromanipulator. The instant method is distinguished over the prior art in using at least a single electrode to provide a highly focused electric field for the fusion of at least two fusion partners. The instant invention is based on a method that allows controllable fusion of single cells. Magae et al. does not address these aspects of the instant invention. Magae et al. do not provide a method of selective electrofusion that comprises bringing the fusion partners in to contact and applying a highly

focused electric field. The method of Magae et al. is a bulk electrofusion, made more efficient by manipulation of the conditions and size of the cell.

As such, Applicants respectfully request withdrawal of the rejection and allowance of the claims.

Claim Rejections- 35 U.S.C. § 102(e)

Claims 1 – 2, 8 – 12, 15 – 19, and 26 – 29 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Pui et al., US Patent No. 6,093,557 (“the ‘557 reference”). The Examiner alleges that the ‘557 reference discloses “a method and apparatus for fusion of cells with vesicles or liposomes that comprises a capillary electrode through which the liposomes are dispersed in a spray on to target cells.” Applicants respectfully submit that the invention as claimed is not anticipated by the ‘557 reference and respectfully traverse the rejection.

The teaching of the ‘557 reference does not anticipate the claimed method for selective electrofusion of at least two fusion partners having cell-like membranes using a highly focused electric field.

The Examiner argues, again, that “the disclosure does not provide a specific and limiting definition of the phrase ‘highly focused’, and the word ‘selective’ is not specifically defined in the disclosure (Office Action, p. 12).” Applicants refer to the arguments presented above, and maintain that the meaning of the term “highly focused” is well-supported and described in the specification, for example, on page 8, lines 30 – 37.

The ‘557 reference fails to teach a method of fusion that is highly focused but, as the examiner points out on page 12 of the Office Action, teaches a “method that establishes a spray of substantially dispersed particles that have an electrical charge applied thereto (col. 3).” The Examiner argues that “the electrospraying method of [the ‘557 reference] is not for the purpose of impact penetration (but that) in addition to the penetration of cells as a result of bombardment, electrospraying techniques can be used to direct liposome droplets over the target cells...to facilitate transfer of material into the cell through fusion (Office Action, p. 12).” The Examiner’s argument does not relate to the claims at hand. In order to anticipate a claim, each and every element of the claim must be found in a single reference. This is discussed in the Manual of Patent Examining Procedure § 2131:

“A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). “The identical invention must be shown in as complete detail as is contained in the . . . claim.” Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an *ipsissimis verbis* test, i.e., identity of terminology is not required. In re Bond, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

In either case, the method of fusion taught by the ‘557 uses a spray that is established in the region of a target that includes one or more cells (see Figure 1A, description). The spray of charged particles provides neither selectivity of fusion between the two partners, nor does it provide an electric field that is highly focused on the fusion partners. The ‘557 reference contains no reference to a highly focused electric field as taught by the instant invention, nor does it mention selectivity of fusion between two fusion partners. Rather, the ‘557 reference teaches a method involving “a spray of substantially dispersed particles (claim 1)” wherein one or more of the substantially dispersed particles is introduced into the target cell.

Accordingly, Applicants respectfully request withdrawal of the rejection and allowance of the claims.

CONCLUSION

In view of the above amendment and remarks, Applicants believe the pending application is in condition for allowance.

Should the Examiner wish to discuss any of the amendments and/or remarks made herein, the undersigned attorney would appreciate the opportunity to do so.

Respectfully submitted,

Date: February 1, 2007



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